General

Guideline Title

Best evidence statement (BESt). Use of *Lactobacillus rhamnosus* GG in children with acute gastroenteritis.

Bibliographic Source(s)

Cincinnati Children's Hospital Medical Center. Best evidence statement (BESt). Use of Lactobacillus rhamnosus GG in children with acute gastroenteritis. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2011 Apr 15. 6 p. [15 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The strength of the recommendation (strongly recommended, recommended, or no recommendation) and the quality of evidence (1a-5) are defined at the end of the "Major Recommendations" field.

It is recommended to administer *Lactobacillus rhamnosus* GG (LGG) to children with acute gastroenteritis to reduce the duration of diarrhea, risk of protracted diarrhea and duration of hospitalization (Szajewska et al., 2007 [1a]; Guarino et al., 2008 [5a]; Local Consensus [5]).

To obtain best efficacy:

- Start LGG treatment as soon as possible
- At a dose of at least 10^{10} colony forming units per day (CFU/day)
- For 5 to 7 days

(Szajewska et al., 2007 [1a]; Guandalini, 2008 [5a]; Guarino et al., 2008 [5a])

Note: The criterion for efficacy of LGG for treatment of acute gastroenteritis is the presence of 10 billion CFU. It is important to determine that the product meets this criterion. One such product readily available locally is Culturelle capsules; Amerifit, Inc. (the product is gluten free but contains milk proteins). Culturelle for Kids contains only 1 billion CFU per dose, and other available probiotic products do not contain the LGG organism. Available in capsules; the contents of the capsules can be dissolved in water for oral administration.

Definitions:

Table of Evidence Levels

Quality Level	Definition
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5	Other: General review, expert opinion, case report, consensus report, or guideline

†a = good quality study; b = lesser quality study

Table of Recommendation Strength

Strength	Definition
"Strongly recommended"	There is consensus that benefits clearly outweigh risks and burdens (or visa-versa for negative recommendations).
"Recommended"	There is consensus that benefits are closely balanced with risks and burdens.
No recommendation made	There is lack of consensus to direct development of a recommendation.
Dimensions: In determining the strength of a recommendation, the development group makes a considered judgment in a consensus process that incorporates critically appraised evidence, clinical experience, and other dimensions as listed below.	
1. Grade of the Body of Evidence (see note above) 2. Safety/Harm 3. Health benefit to patient (direct benefit) 4. Burden to patient of adherence to recommendation (cost, hassle, discomfort, pain, motivation, ability to adhere, time) 5. Cost-effectiveness to healthcare system (balance of cost/savings of resources, staff time, and supplies based on published studies or onsite analysis) 6. Directness (the extent to which the body of evidence directly answers the clinical question [population/problem, intervention, comparison, outcome]) 7. Impact on morbidity/mortality or quality of life	

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Acute gastroenteritis

Guideline Category

Treatment

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Pediatrics

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate in children with acute gastroenteritis (AGE) if the use of *Lactobacillus rhamnosus* GG in addition to oral rehydration solution (ORS) compared to ORS alone is effective in reducing the duration of diarrhea

Target Population

Included

Overall healthy children aged 2 months to 18 years with acute gastroenteritis (AGE)*, with or without fever or vomiting

*AGE is defined as a decrease in the consistency of stools and/or an increase in the frequency of evacuations (≥3/day) lasting less than 7 days.

Excluded

- Children with underlying chronic diseases (mainly immunocompromised patients, and including debilitated state or malignancies and chronic conditions that can increase intestinal mucosal permeability)
- Premature infants

Interventions and Practices Considered

Lactobacillus rhamnosus GG in addition to oral rehydration solution (ORS) compared to ORS alone

Major Outcomes Considered

- Duration of diarrhea
- Risk of protracted diarrhea
- Duration of hospitalization

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Search Strategy

1. Databases: MEDLINE, Cochrane Database of Systematic Reviews
   Search Terms: gastroenteritis/tw, gastroenteritis/MeSH
   acute diarrhea/MeSH, acute diarrhea/tw
   probiotic/tw, probiotics/MeSH
   Lactobacillus/tw, Lactobacillus/MeSH
   child*

   Filters: Publication date: 1980 to present
   humans
   English language
   "all child (0 to 18 years)"
2. Additional articles identified by the author and ad hoc reviewers
3. Additional articles identified from reference lists of reviewed articles

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Table of Evidence Levels

Quality Level	Definition
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5	Other: General review, expert opinion, case report, consensus report, or guideline

†a = good quality study; b = lesser quality study

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Table of Recommendation Strength

Strength	Definition
"Strongly recommended"	There is consensus that benefits clearly outweigh risks and burdens (or visa-versa for negative recommendations).
"Recommended"	There is consensus that benefits are closely balanced with risks and burdens.
No recommendation made	There is lack of consensus to direct development of a recommendation.
Dimensions: In determining the strength of a recommendation, the development group makes a considered judgment in a consensus process that incorporates critically appraised evidence, clinical experience, and other dimensions as listed below.	
1. Grade of the Body of Evidence (see note above) 2. Safety/Harm 3. Health benefit to patient (direct benefit) 4. Burden to patient of adherence to recommendation (cost, hassle, discomfort, pain, motivation, ability to adhere, time) 5. Cost-effectiveness to healthcare system (balance of cost/savings of resources, staff time, and supplies based on published studies or onsite analysis) 6. Directness (the extent to which the body of evidence directly answers the clinical question [population/problem, intervention, comparison, outcome]) 7. Impact on morbidity/mortality or quality of life	

Cost Analysis

The recommendations suggested in this best evidence statement (BESt) have a good applicability in daily clinical practice due to likelihood for a positive cost-benefit ratio for probiotic use in acute gastroenteritis, when including hospitalization and emergency department readmission rates.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

Reviewed by two independent reviewers against established criteria

Evidence Supporting the Recommendations

References Supporting the Recommendations

Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. Cochrane Database Syst Rev. 2010; (11):CD003048. PubMed

Cincinnati Children's Hospital Medical Center. Evidence-based clinical care guideline for acute gastroenteritis (AGE) in children aged 2 months through 5 years. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2006 May. 15 p. [50 references]

Guandalini S. Probiotics for children with diarrhea: an update. J Clin Gastroenterol. 2008 Jul;42 Suppl 2:S53-7. [24 references] PubMed

Guarino A, Albano F, Ashkenazi S, Gendrel D, Hoekstra JH, Shamir R, Szajewska H, ESPGHAN/ESPID Evidence-Based Guidelines for the Management of Acute Gastroenteritis [trunc]. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: executive summary. J Pediatr Gastroenterol Nutr. 2008 May;46(5):619-21. PubMed

Szajewska H, Skorka A, Ruszczynski M, Gieruszczak-Bialek D. Meta-analysis: Lactobacillus GG for treating acute diarrhoea in children. Aliment Pharmacol Ther. 2007 Apr 15;25(8):871-81. [52 references] PubMed

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The health benefits for *Lactobacillus rhamnosus* GG (LGG) administration in adjunct to oral rehydration solution (ORS) consist of reduction of diarrhea duration, reduction in risk of having a protracted diarrhea, and reduction of duration of hospitalization.
- Indirectly, the use of LGG could lead to a reduction of acute gastroenteritis-related costs in term of work days lost by the family and days of hospitalization; and the routine use of LGG in inpatients and community children with acute diarrhea could reduce the exposure to nosocomial and daycare infection.

Potential Harms

Side Effects

Probiotics are generally regarded as safe, and side effects in ambulatory care have rarely been reported. Bacterial translocation, sepsis, and the risk of carrying antibiotic resistance plasmids that may spread resistance to antibiotics have been reported. The latter has been reported for some probiotics, such as *Lactobacillus reuteri* ATCC 55730 and *Enterococcus faecium*, but not for *Lactobacillus rhamnosus* GG (LGG).

Risks

The risk for bacteremia and sepsis after LGG ingestion has been reported in some case reports involving infants and children with severe underlying diseases like short-gut syndrome, prematurity, cerebral palsy or cardiac surgical diseases; all these children required parenteral nutrition through central venous catheter or jejunostomy feeding. No risks have been reported by using LGG in cohorts of children with acute gastroenteritis involved in clinical trials.

Qualifying Statements

Qualifying Statements

This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

Implementation of the Guideline

Description of Implementation Strategy

Cincinnati Children's Hospital Medical Center (CCHMC) will use a rapid *Quality Improvement* strategy aimed to increase the rate of administration of *Lactobacillus rhamnosus* GG (LGG) in hospitalized preschool children with acute gastroenteritis (AGE), with the final objective to reduce the duration of hospitalization and the rate of readmission to the emergency department in children with AGE by reducing the duration of diarrhea.

The primary intervention will be education of medical and non-medical personnel working in selected units and involved in the management of children with AGE (attending physicians, fellows, residents, nurses, pharmacists, and families).

The intervention will be focused on the following points:

- Education of physicians and nurses to improve the knowledge of evidence for probiotic use in AGE
- Interaction with the pharmacy service to ensure availability of LGG in the appropriate formulation for inpatients
- Standardization of LGG administration (time, dose, frequency, and duration of the therapy)
- Education of the family to ensure correct home therapy

As the baseline value the guideline developers will use the percentage of children, aged 2 months to 5 years, receiving LGG for treatment of AGE in the previous 13 months, in the same inpatient units as are used for the intervention. The guideline developers will assess, with a weekly measurement during the next 6 months, the variation of the percentage of preschool children receiving LGG during hospitalization.

Implementation Tools

Audit Criteria/Indicators

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Cincinnati Children's Hospital Medical Center. Best evidence statement (BESt). Use of Lactobacillus rhamnosus GG in children with acute gastroenteritis. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2011 Apr 15. 6 p. [15 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Apr 15

Guideline Developer(s)

Cincinnati Children's Hospital Medical Center - Hospital/Medical Center

Source(s) of Funding

Cincinnati Children's Hospital Medical Center

Guideline Committee

Not stated

Composition of Group That Authored the Guideline

Group/Team Leader: Andrea Lo Vecchio, MD, Resident in Pediatrics, Department of Pediatrics - University of Naples "Federico II", Italy

Ad hoc Reviewers and Support Personnel: Eloise Clark, MPH, MBA, EBDM Program Administrator, Anderson Center for Health Systems Excellence; Patrick Conway, MD, MSc, Director of Hospital Medicine & EBDM; Wendy Engstrom Gerhardt, MSN, RN-BC, EBDM Program Administrator, Anderson Center for Health Systems Excellence; Trina Hemmelgarn, Pharm D, Pharmacist; Srikant Iyer, MD, MPH, Emergency Department; Betsy List, MPH, RN, EBDM Program Administrator, Anderson Center for Health Systems Excellence; Joshua Schaffzin, MD, Pediatric Hospitalist; Karen Vonderhaar, MS, RN, EBDM Program Administrator, Anderson Center for Health Systems Excellence; Connie Yau, Clinical Research Coordinator, Hospital Medicine

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Cincinnati Children's Hospital Medical Center .

Print copies: For information regarding the full-text guideline, print copies, or evidence-based practice support services contact the Cincinnati Children's Hospital Medical Center Health James M. Anderson Center for Health Systems Excellence at EBDMInfo@cchmc.org.

Availability of Companion Documents

The following are available:

- Judging the strength of a recommendation. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2008 Jan. 1 p. Available from the Cincinnati Children's Hospital Medical Center .
- Grading a body of evidence to answer a clinical question. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 1 p. Available from the Cincinnati Children's Hospital Medical Center .
- Table of evidence levels. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2008 Feb 29. 1 p. Available from the Cincinnati Children's Hospital Medical Center .

Print copies: For information regarding the full-text guideline, print copies, or evidence-based practice support services contact the Cincinnati Children's Hospital Medical Center Health James M. Anderson Center for Health Systems Excellence at EBDMInfo@cchmc.org.

In addition, proposed process and outcome measures are available in the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on September 22, 2011.

Copyright Statement

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion-criteria.aspx.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.